

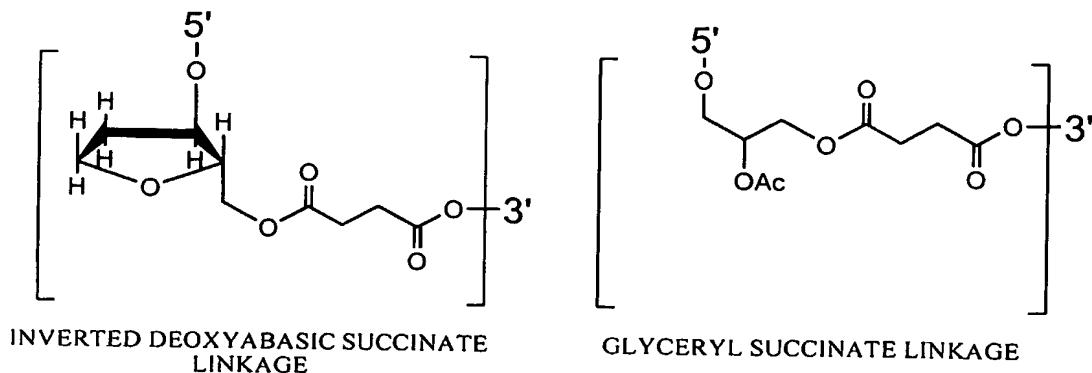
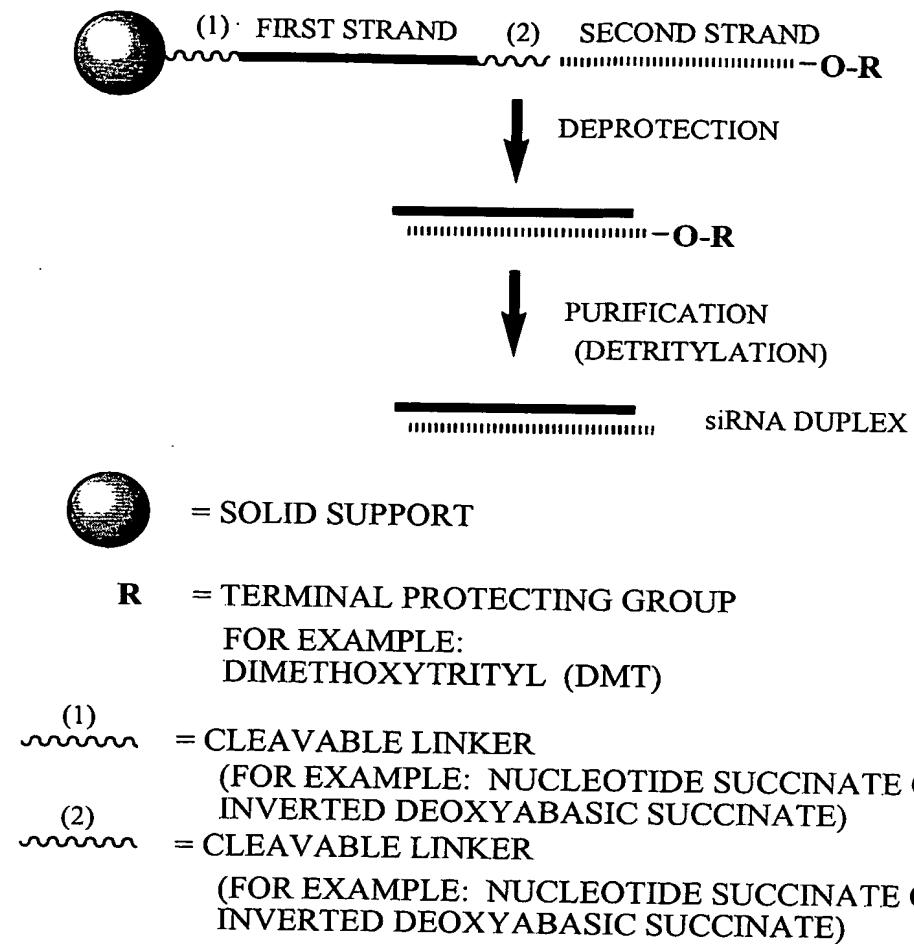
Figure 1

Figure 2

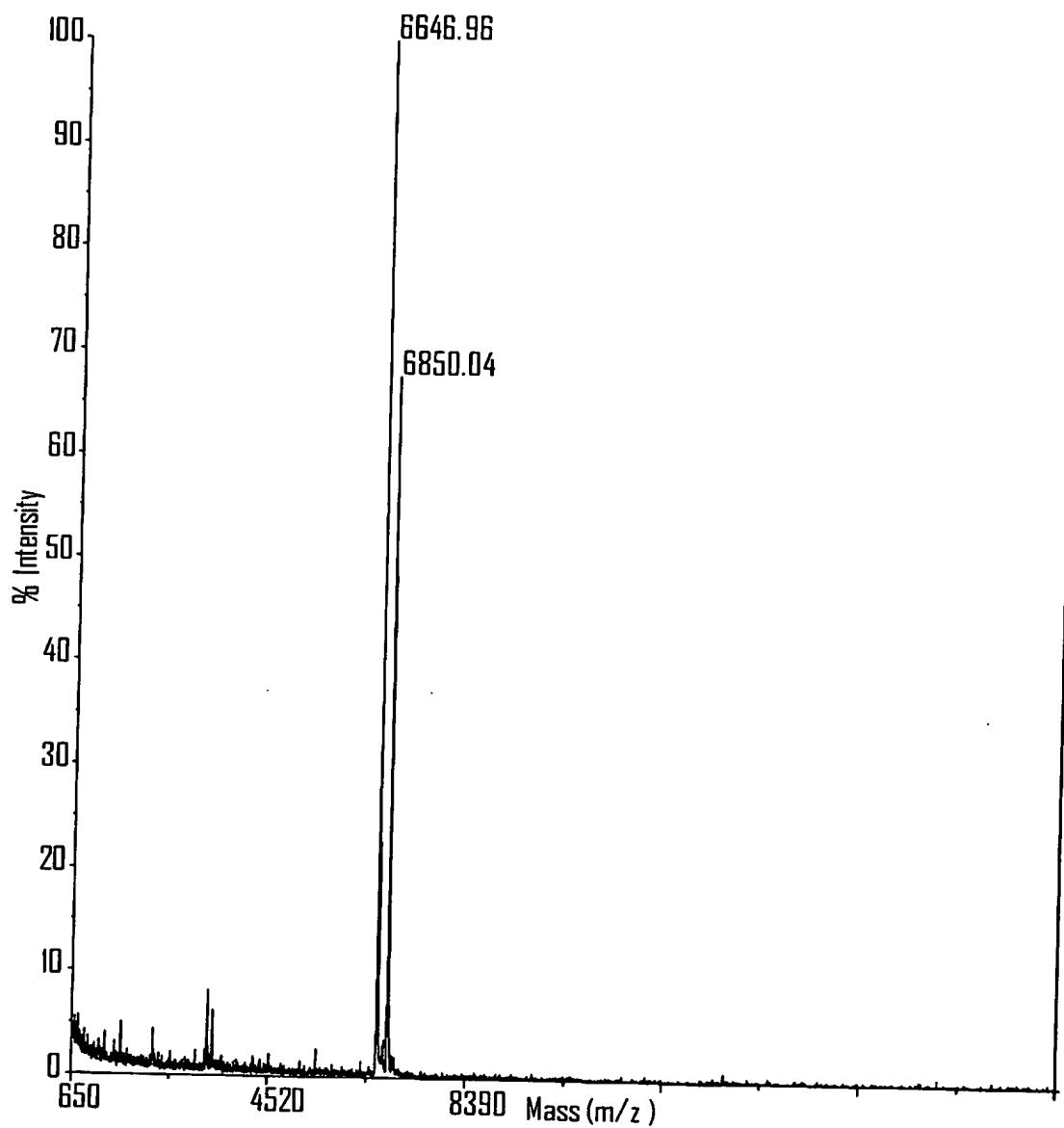


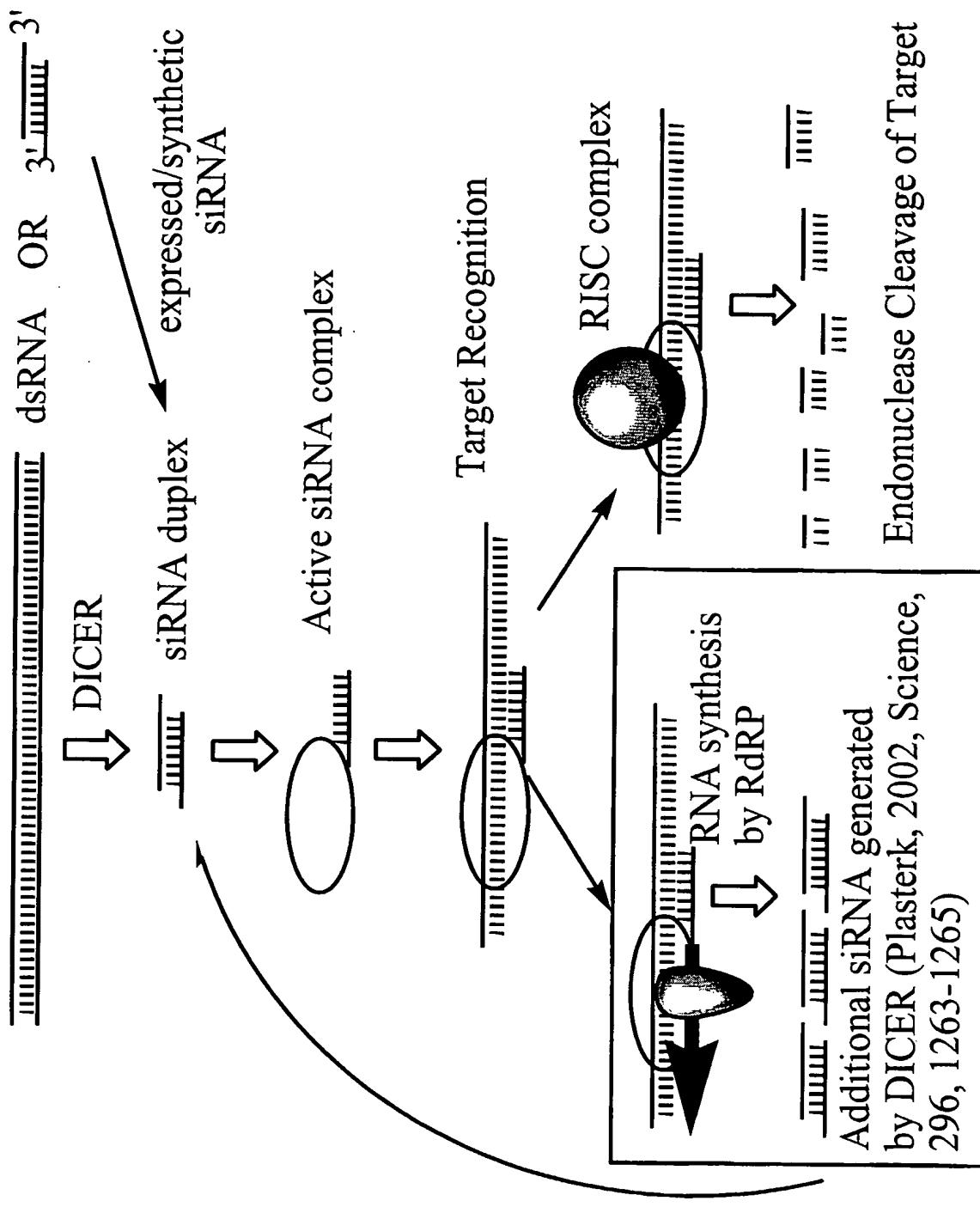
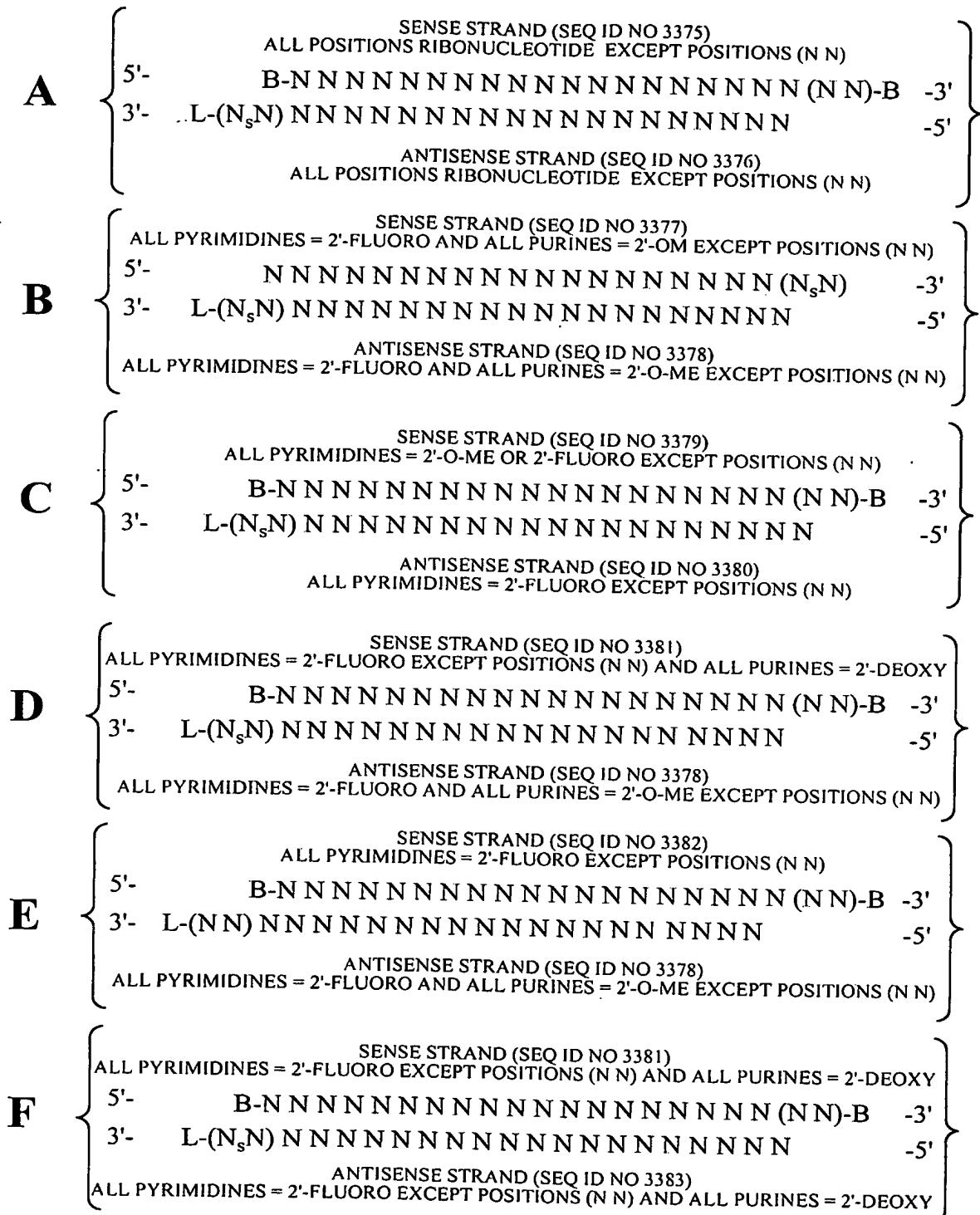
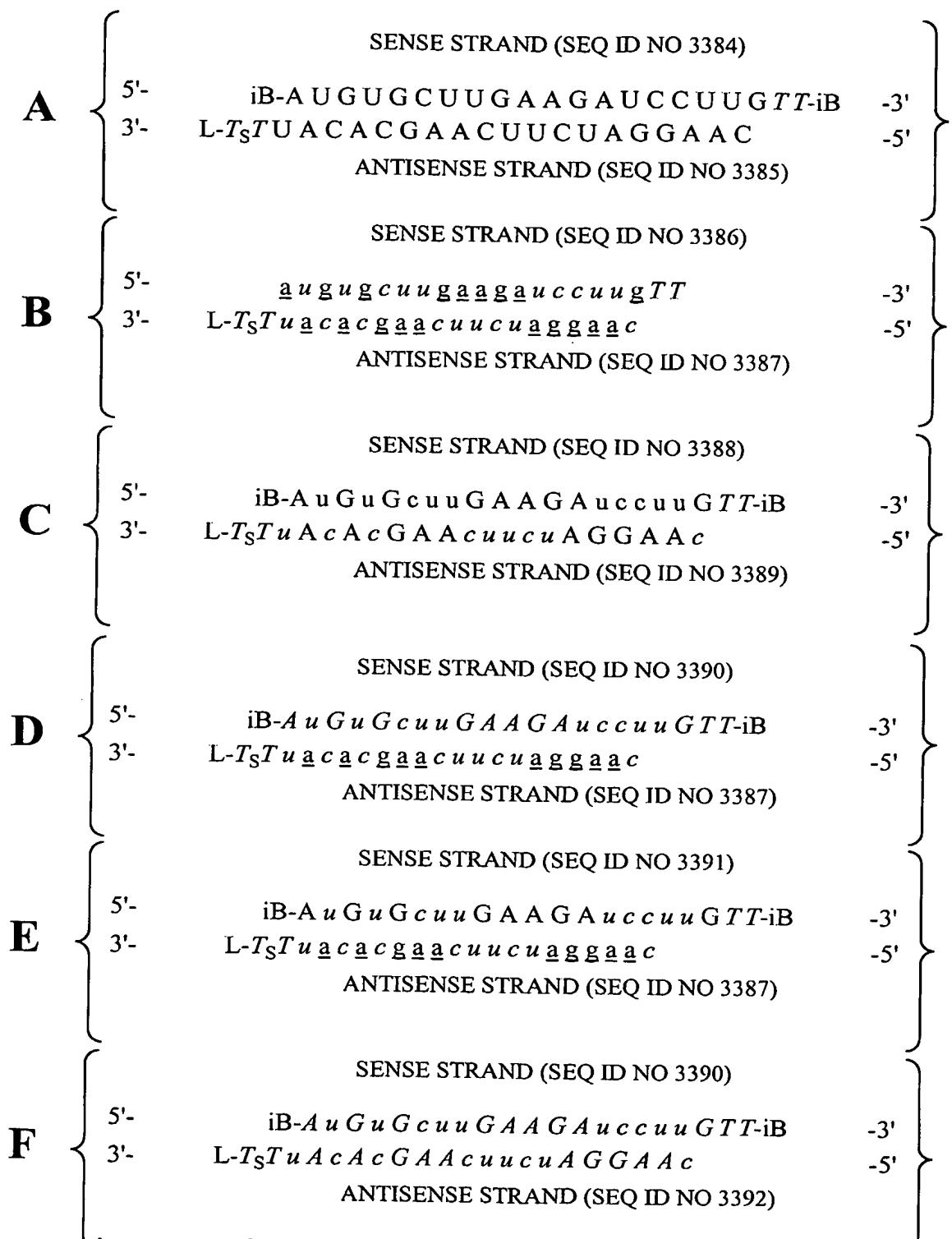
Figure 3

Figure 4



POSITIONS (NN) CAN COMprise ANY NUCLEOTIDE, SUCH AS DEOXYNUCLEOTIDES (eg. THYMIDINE) OR UNIVERSAL BASES B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP THAT IS OPTIONALy PRESENTL = GLYCERYL or B THAT IS OPTIONALy PRESENTS = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE that is optionaly absent

Figure 5

lower case = 2'-O-Methyl or 2'-deoxy-2'-fluoro

italic lower case = 2'-deoxy-2'-fluoro

underline = 2'-O-methyl

ITALIC UPPER CASE = DEOXYiB = INVERTED
 DEOXYABASICL = GLYCERYL MOIETY or iB
 OPTIONAL PRESENTS = PHOSPHOROTHIOATE C
 PHOSPHORODITHIOATE OPTIONAL PRESEN

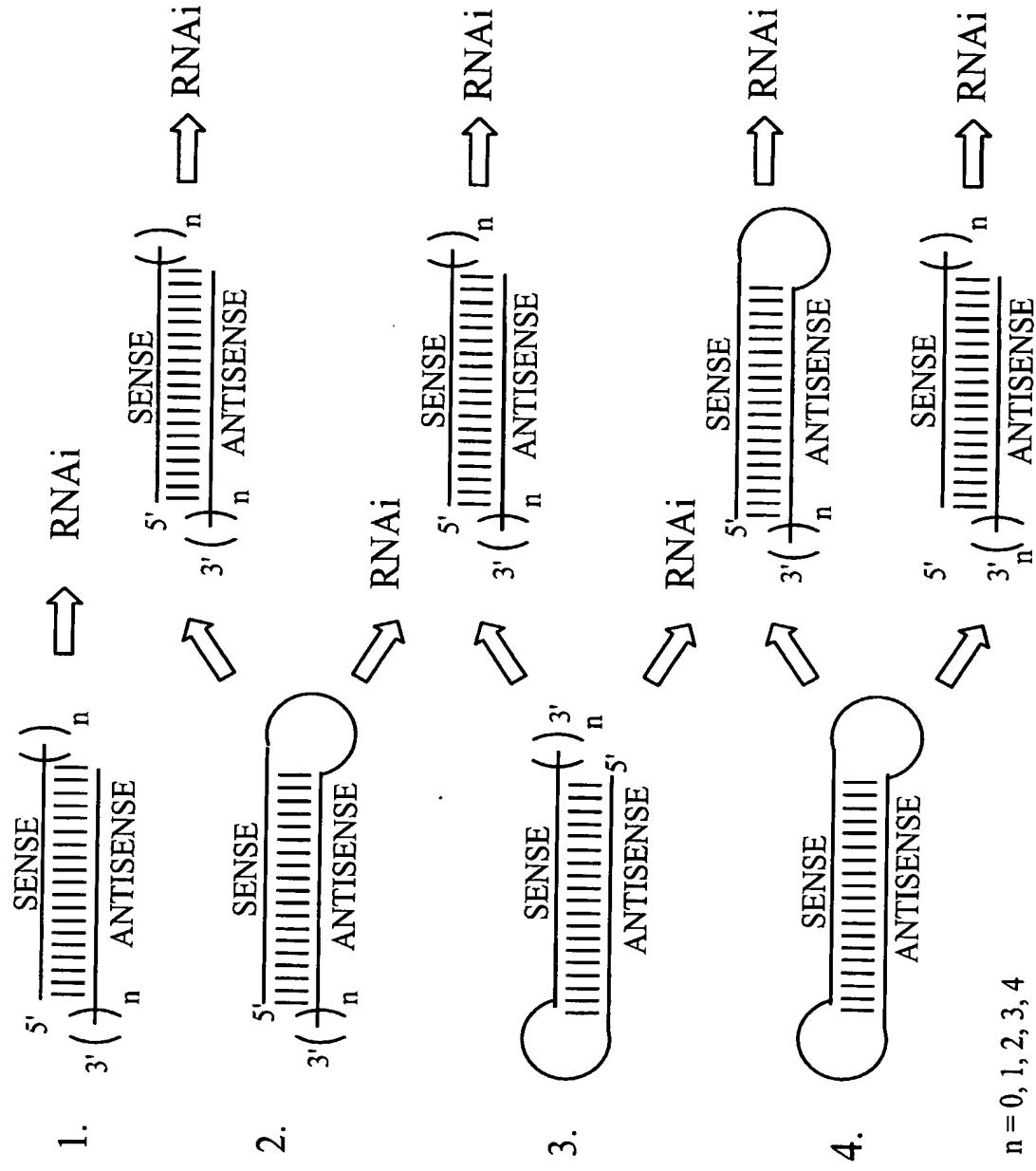
Figure 6

Figure 7

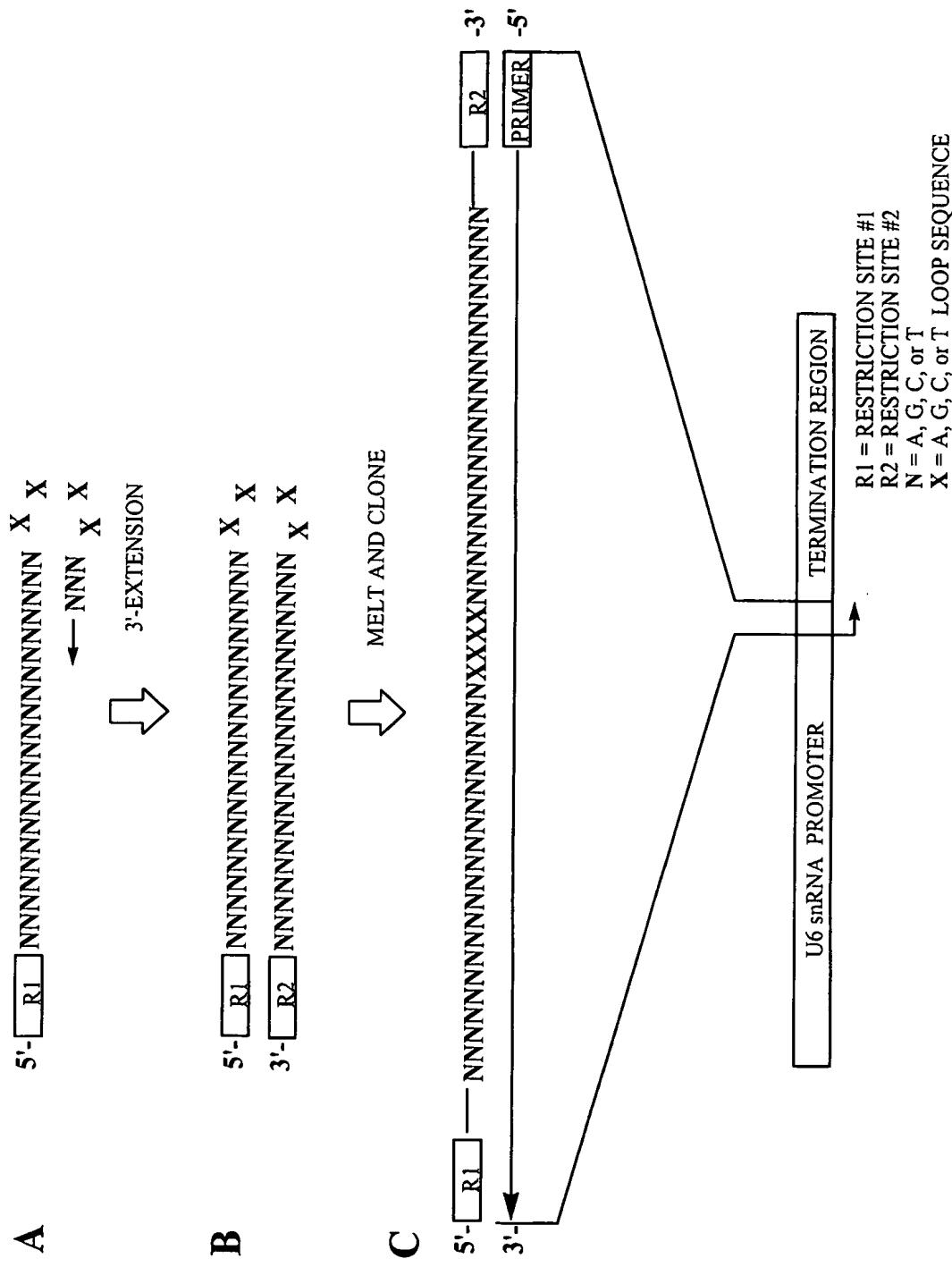


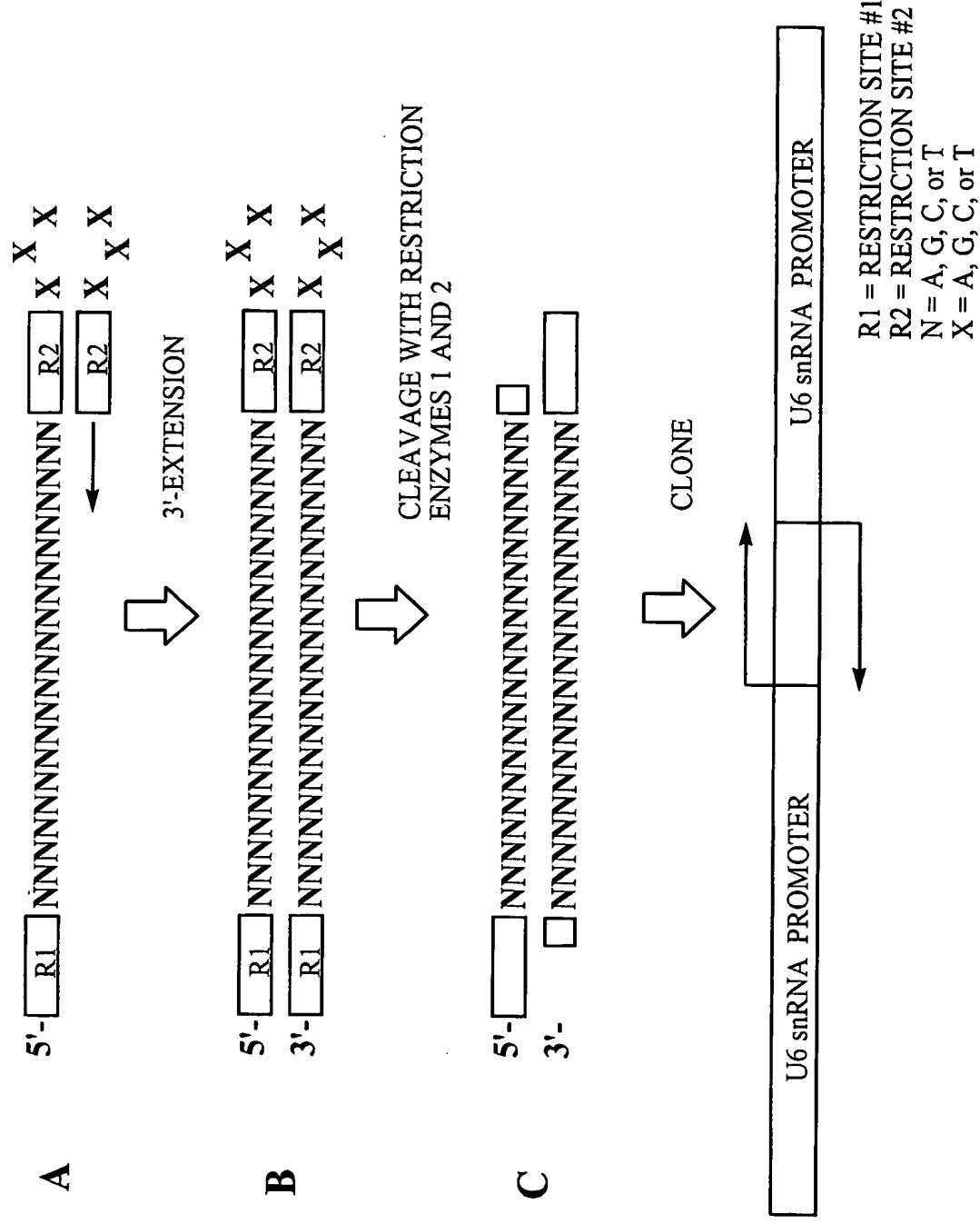
Figure 8

Figure 9: Target site Selection using siRNA

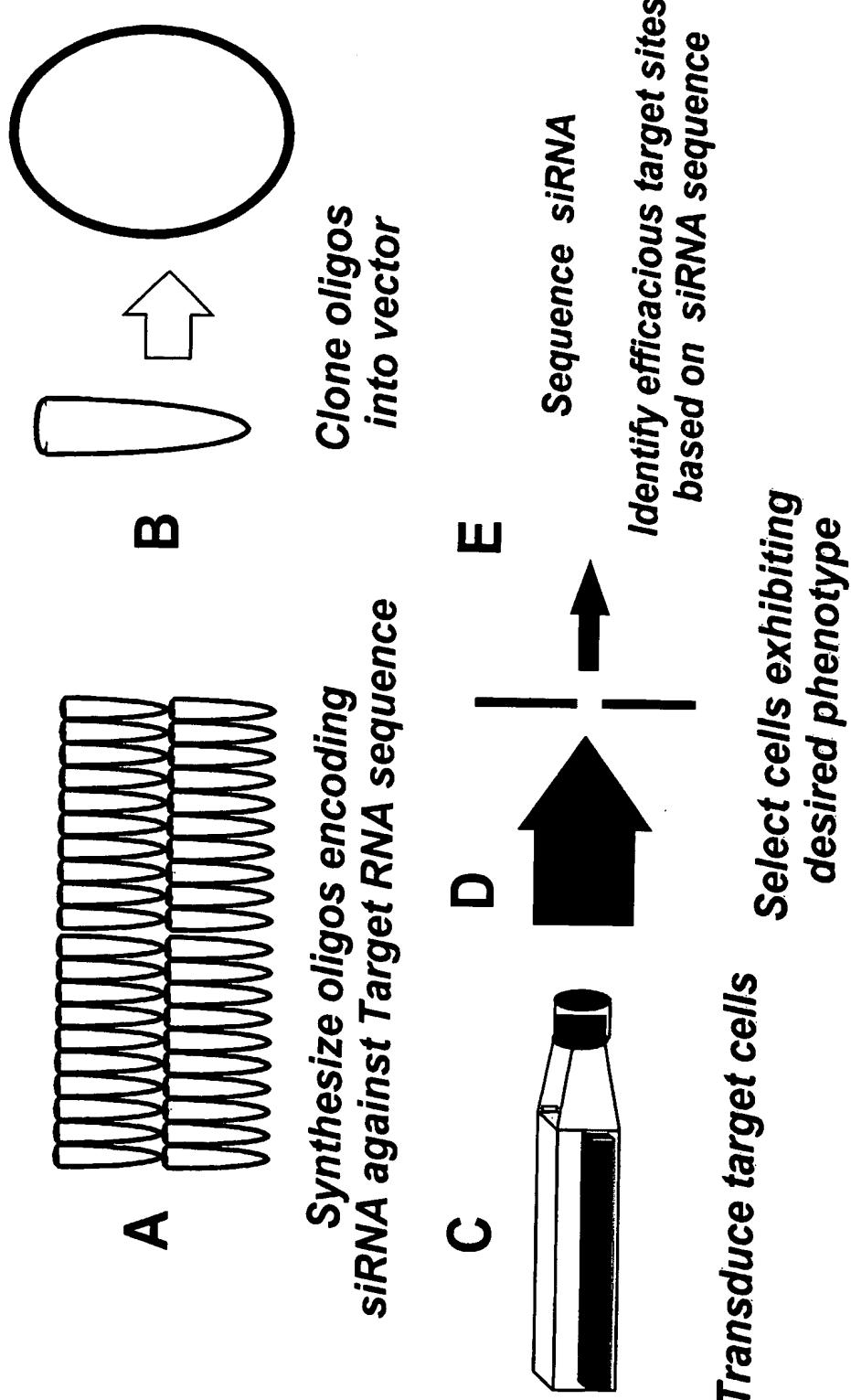
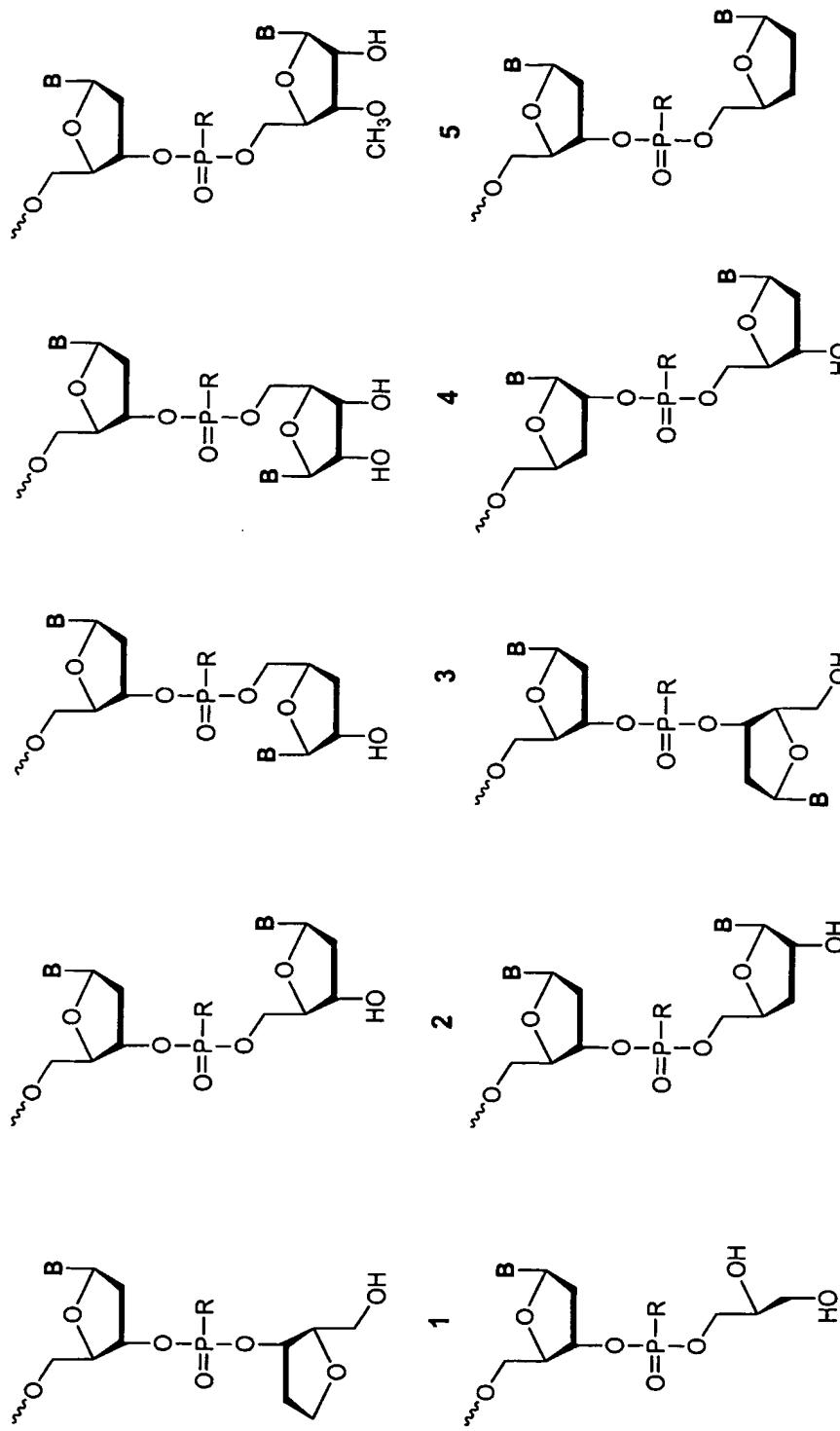


Figure 10

$\text{R} = \text{O}, \text{S}, \text{N}$, alkyl, substituted alkyl, O-alkyl, S-alkyl, alkaryl, or aralkyl
 $\text{B} = \text{Independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).}$

Figure 11: Modification Strategy

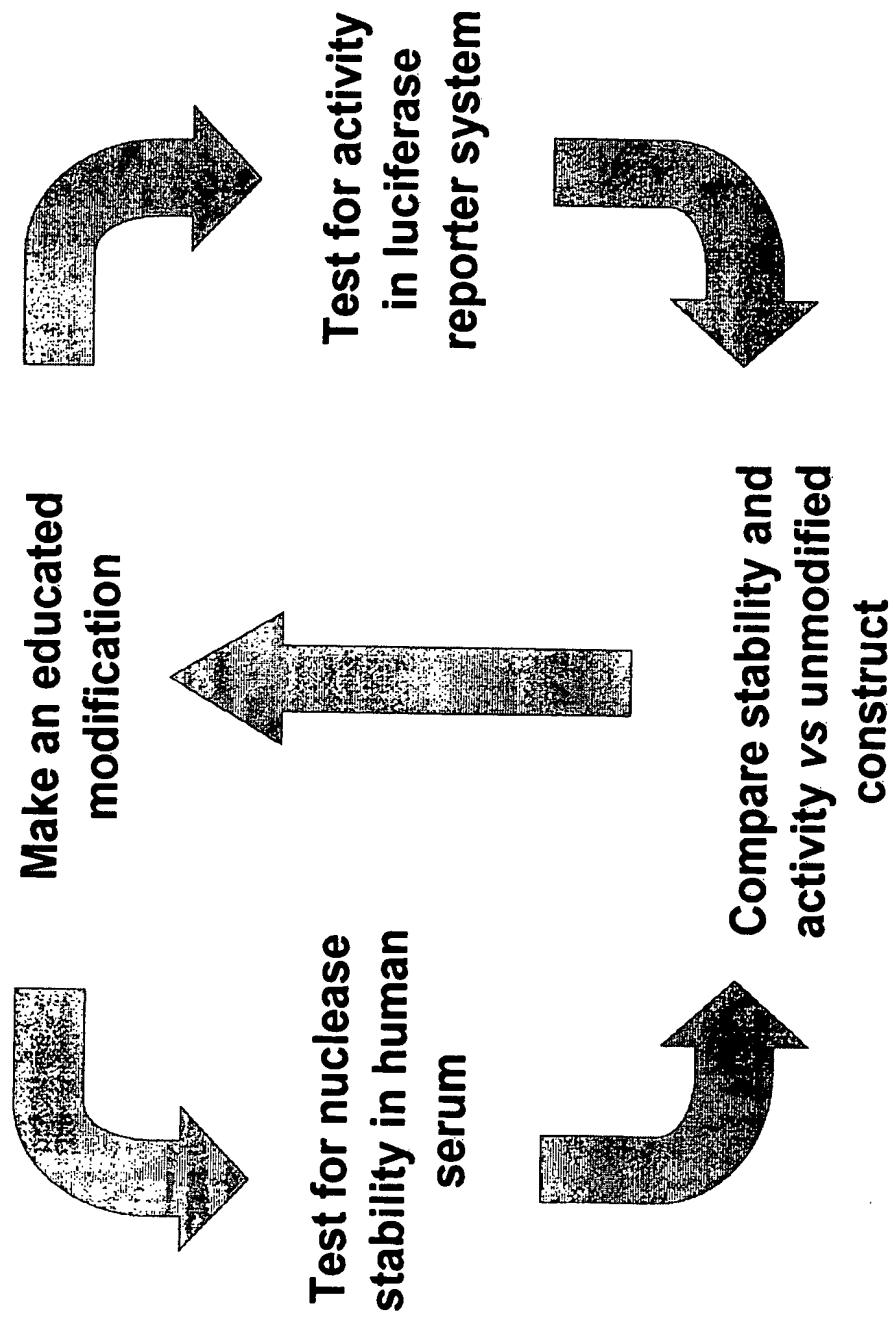


Figure 12: Phosphorylated siNA constructs

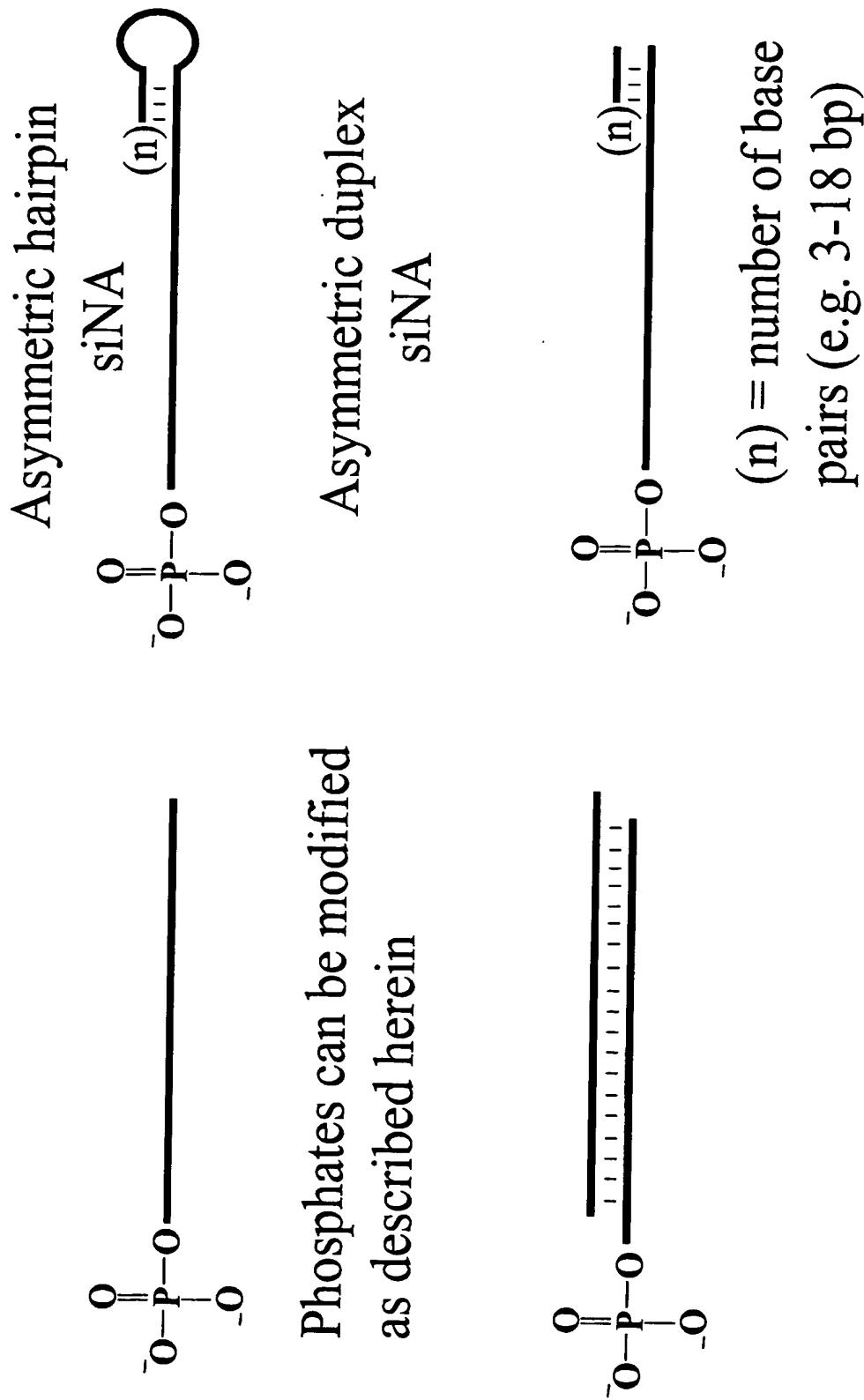


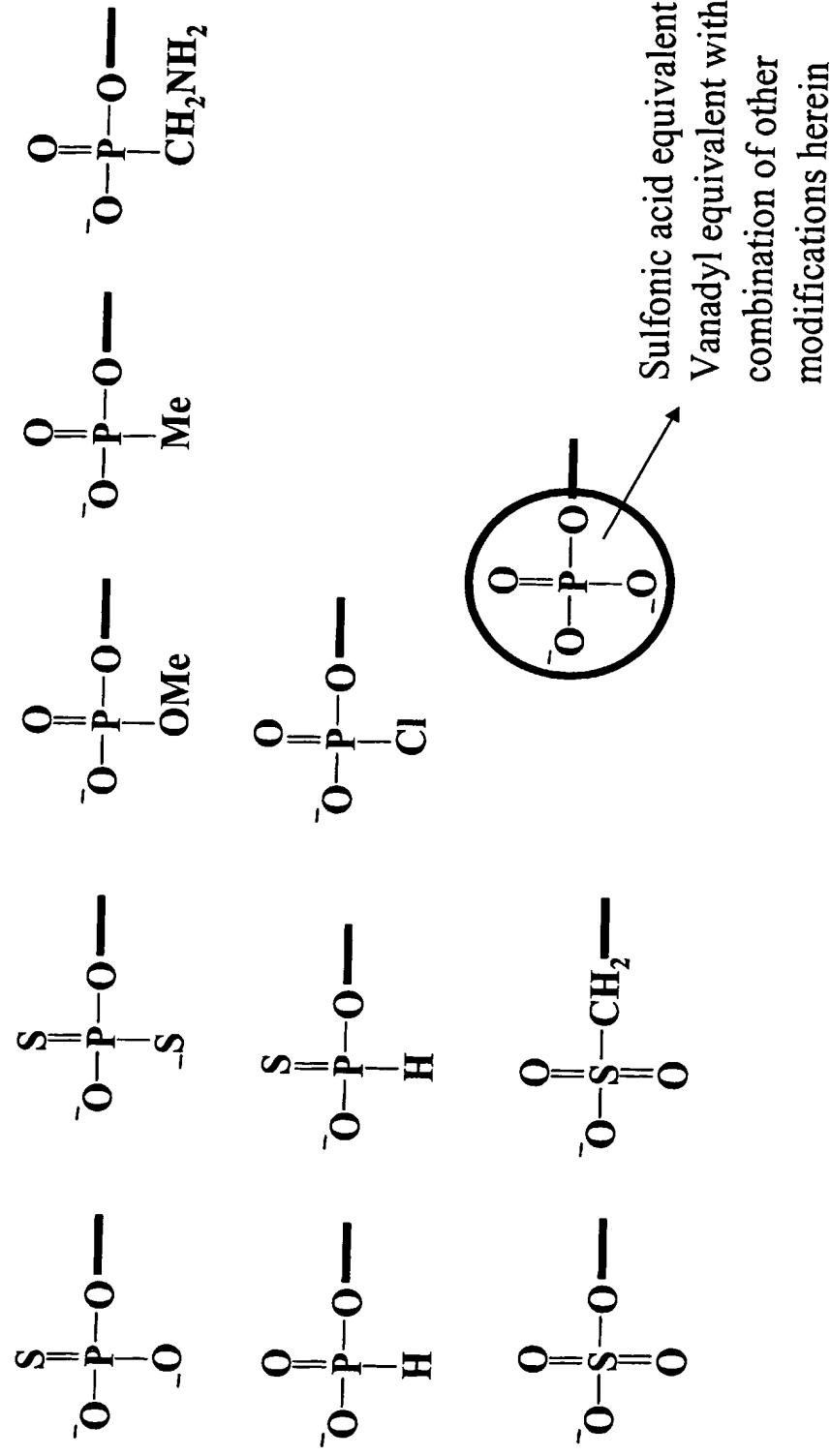
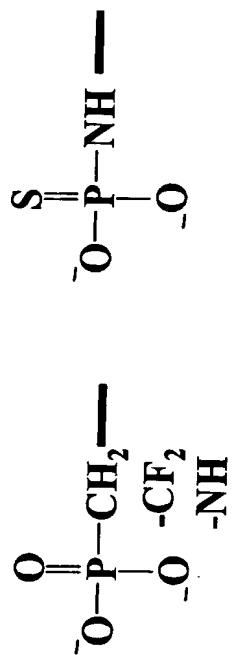
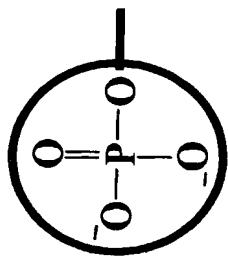
Figure 13: 5'-phosphate modifications

Figure 14A: Duplex forming oligonucleotide constructs that utilize palindrome or repeat sequences

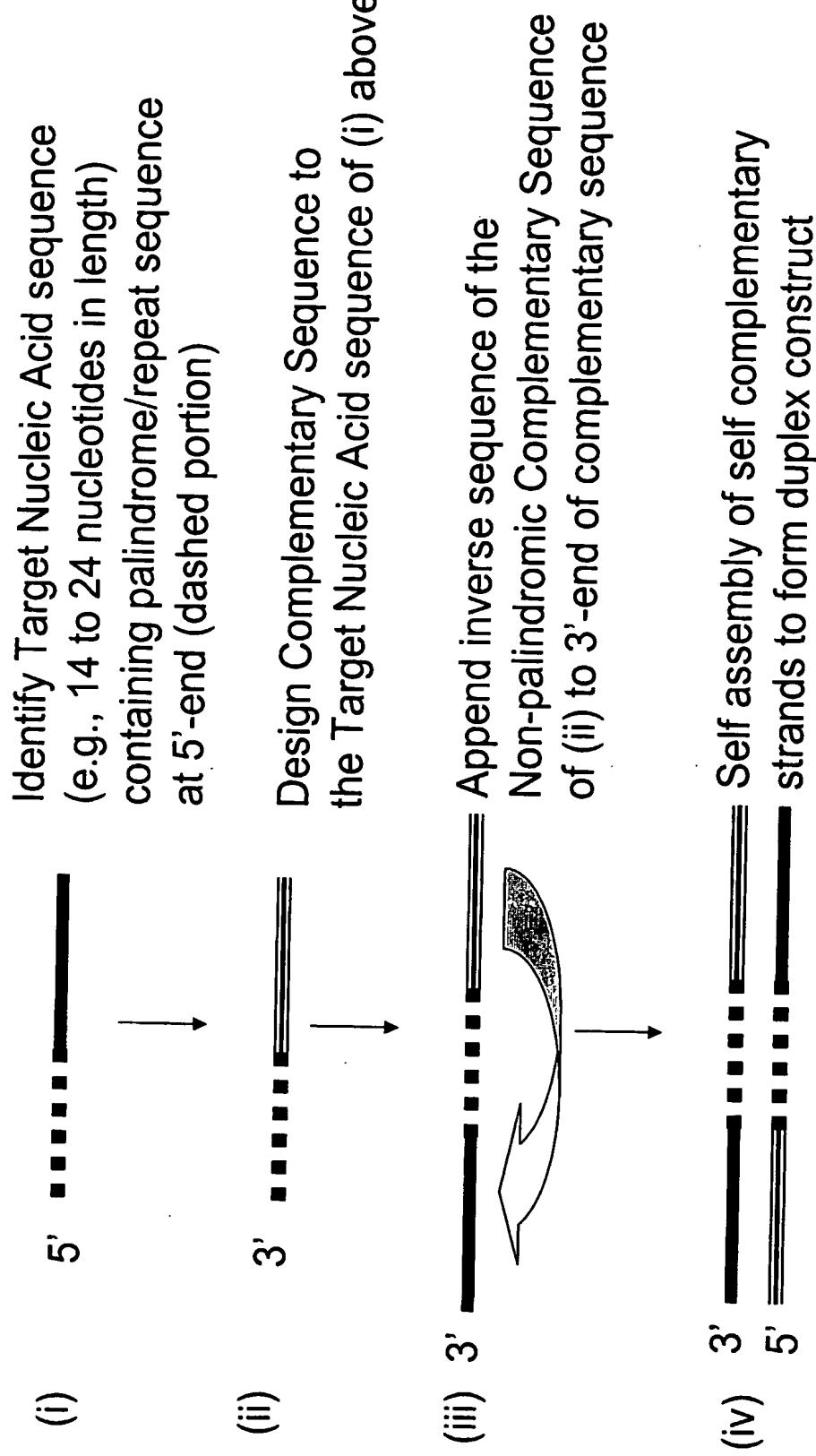


Figure 14B: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence

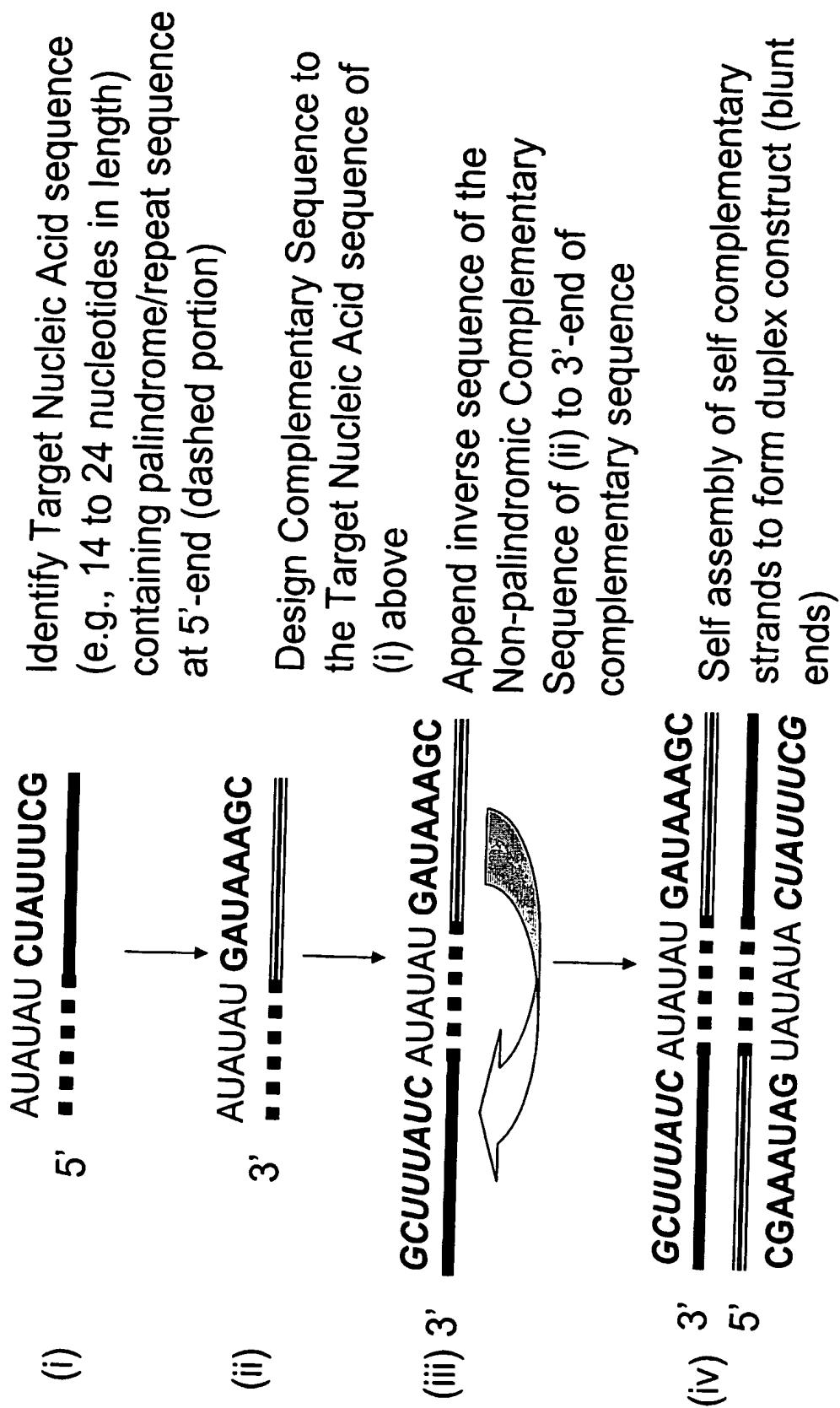


Figure 14C: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly

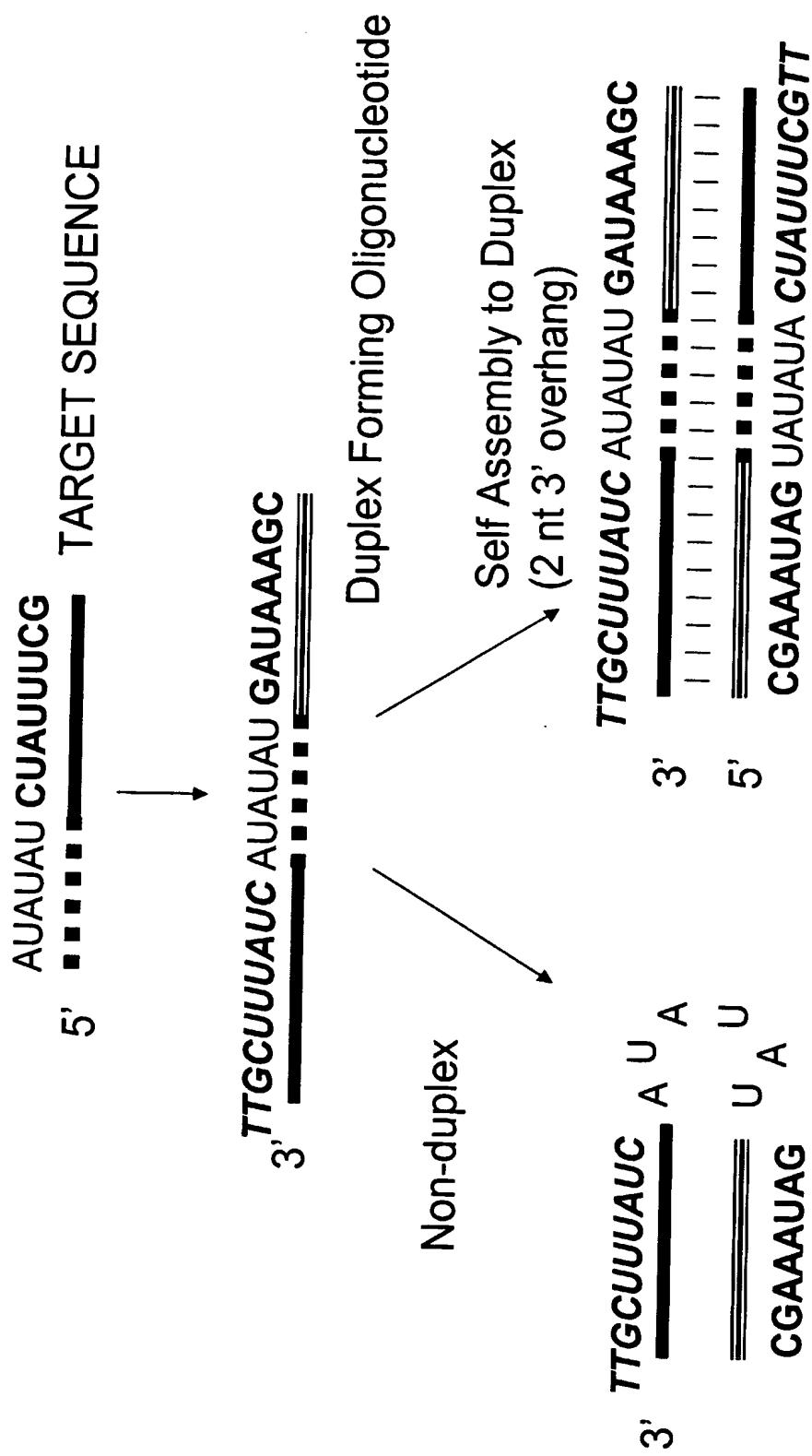


Figure 14D: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly and inhibition of Target Sequence Expression

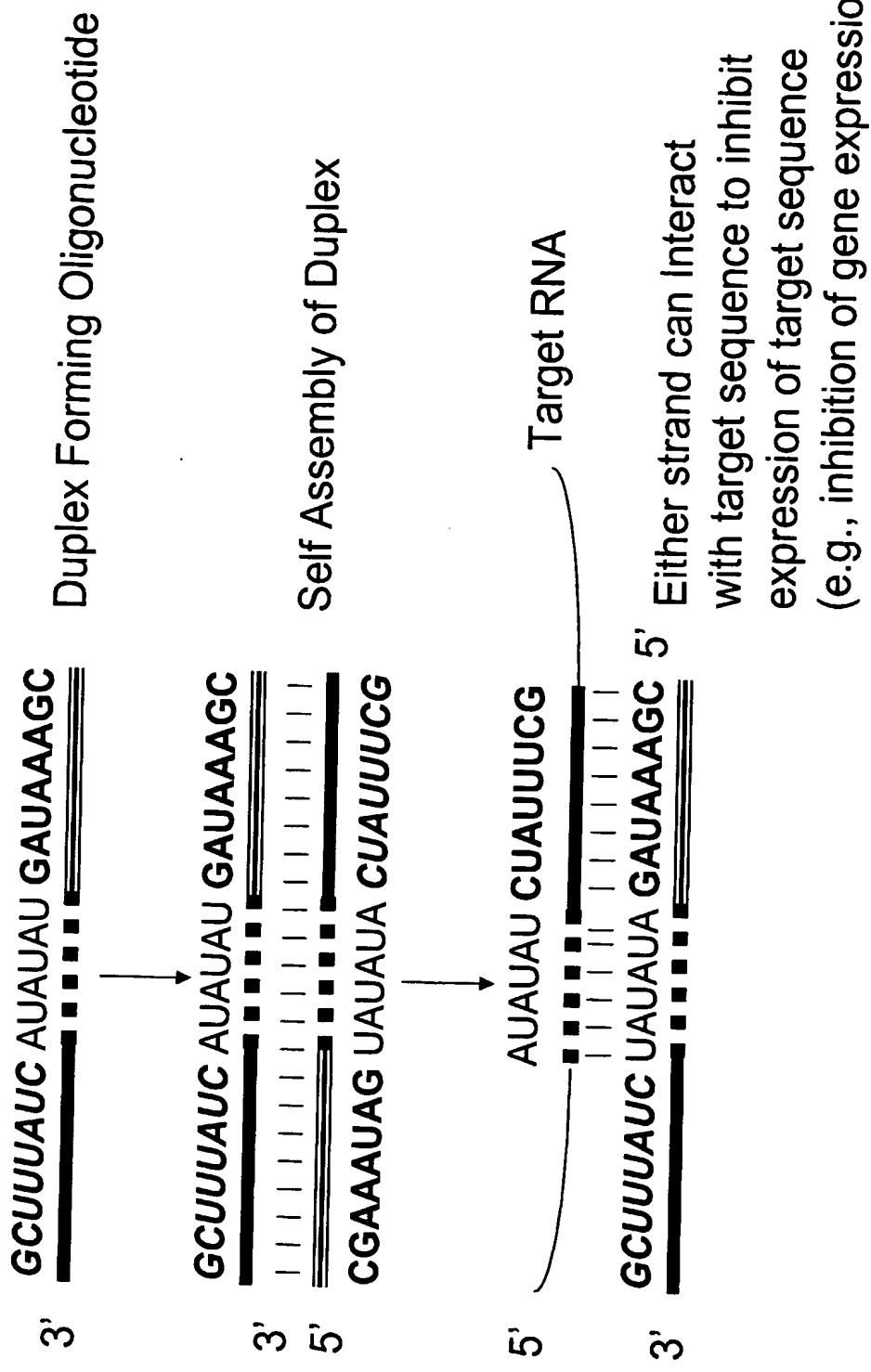


Figure 15: Duplex forming oligonucleotide constructs that utilize artificial palindrome or repeat sequences

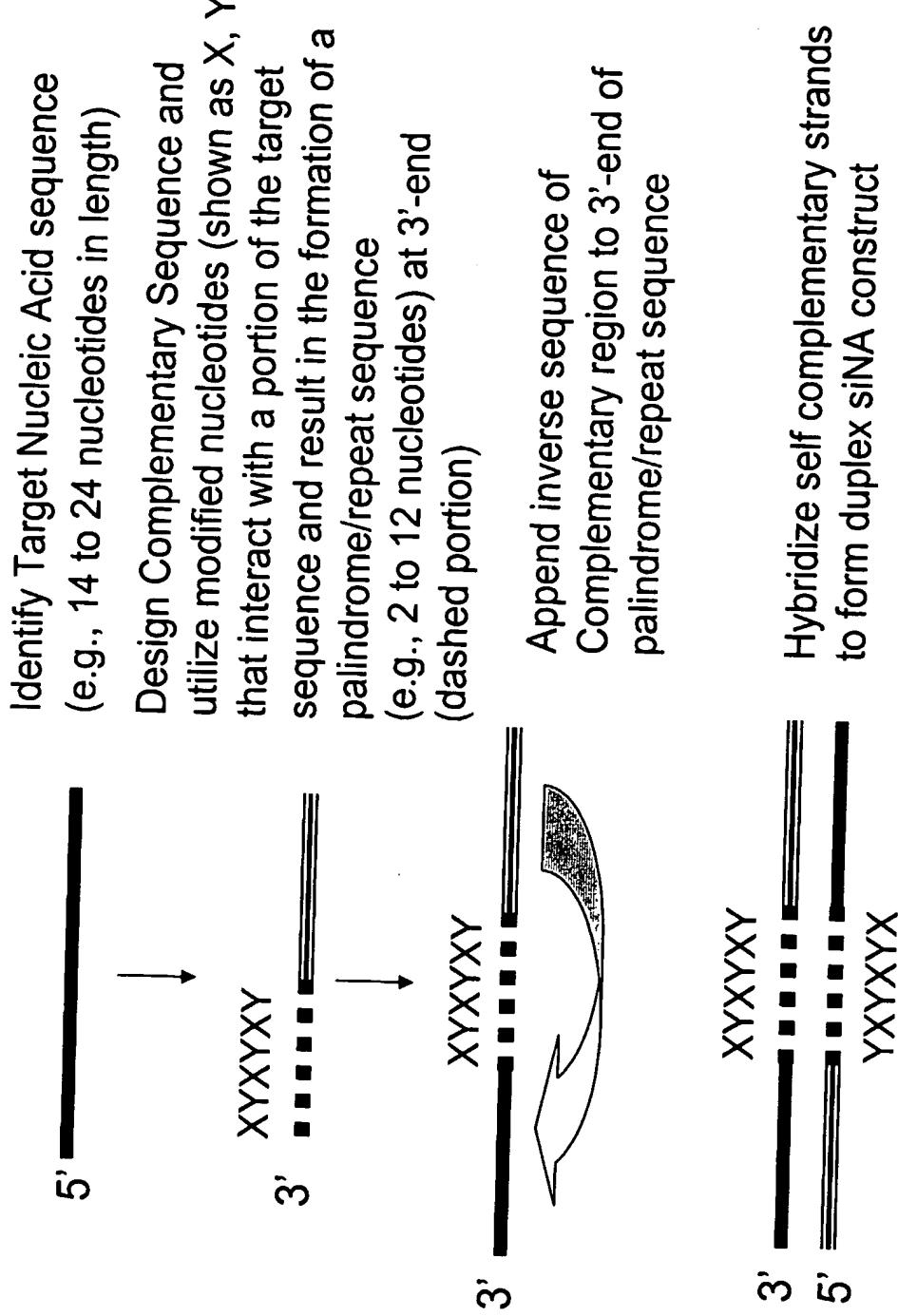


Figure 16: Examples of double stranded multifunctional siNA constructs with distinct complementary regions

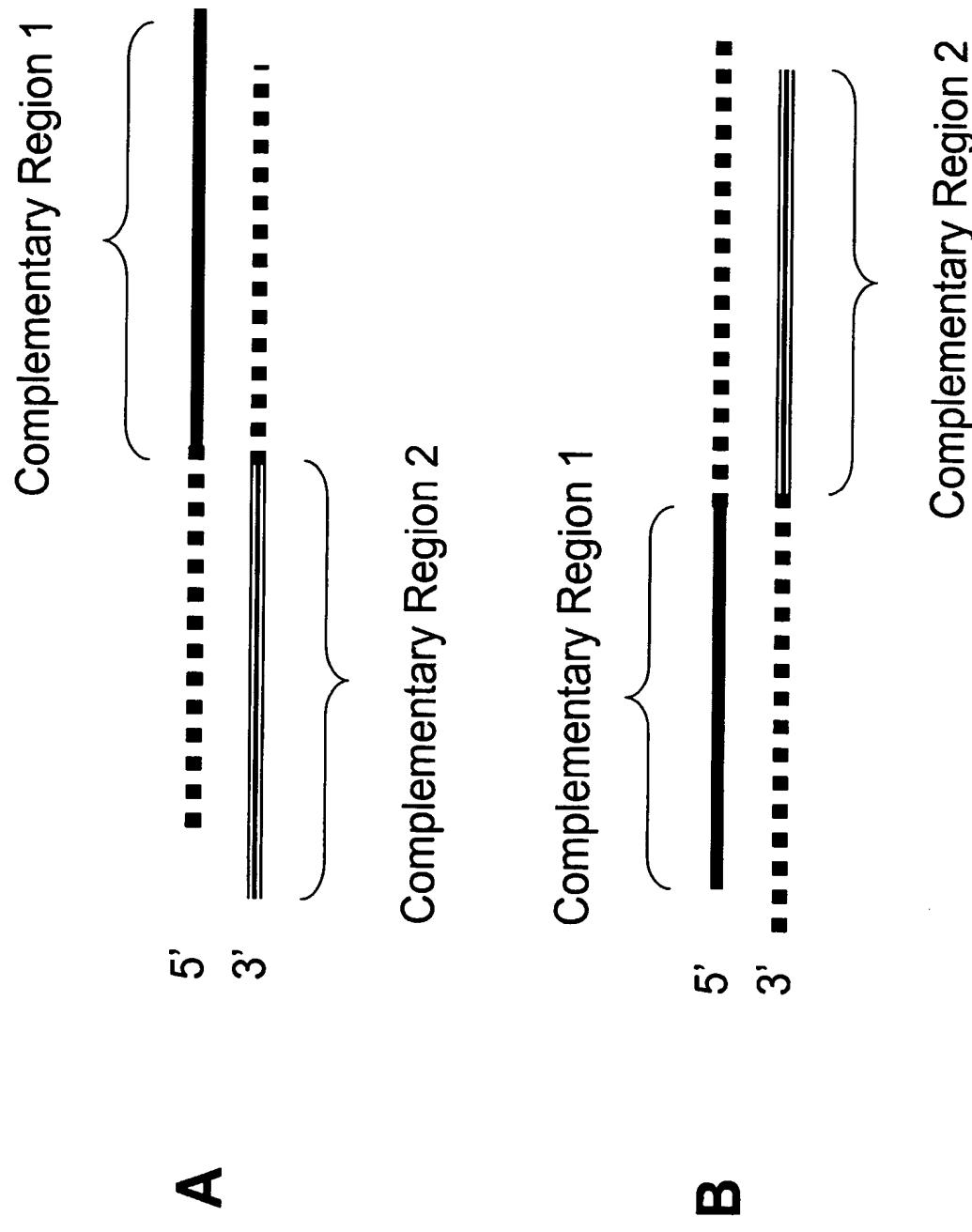


Figure 17: Examples of hairpin multifunctional siNA constructs with distinct complementary regions

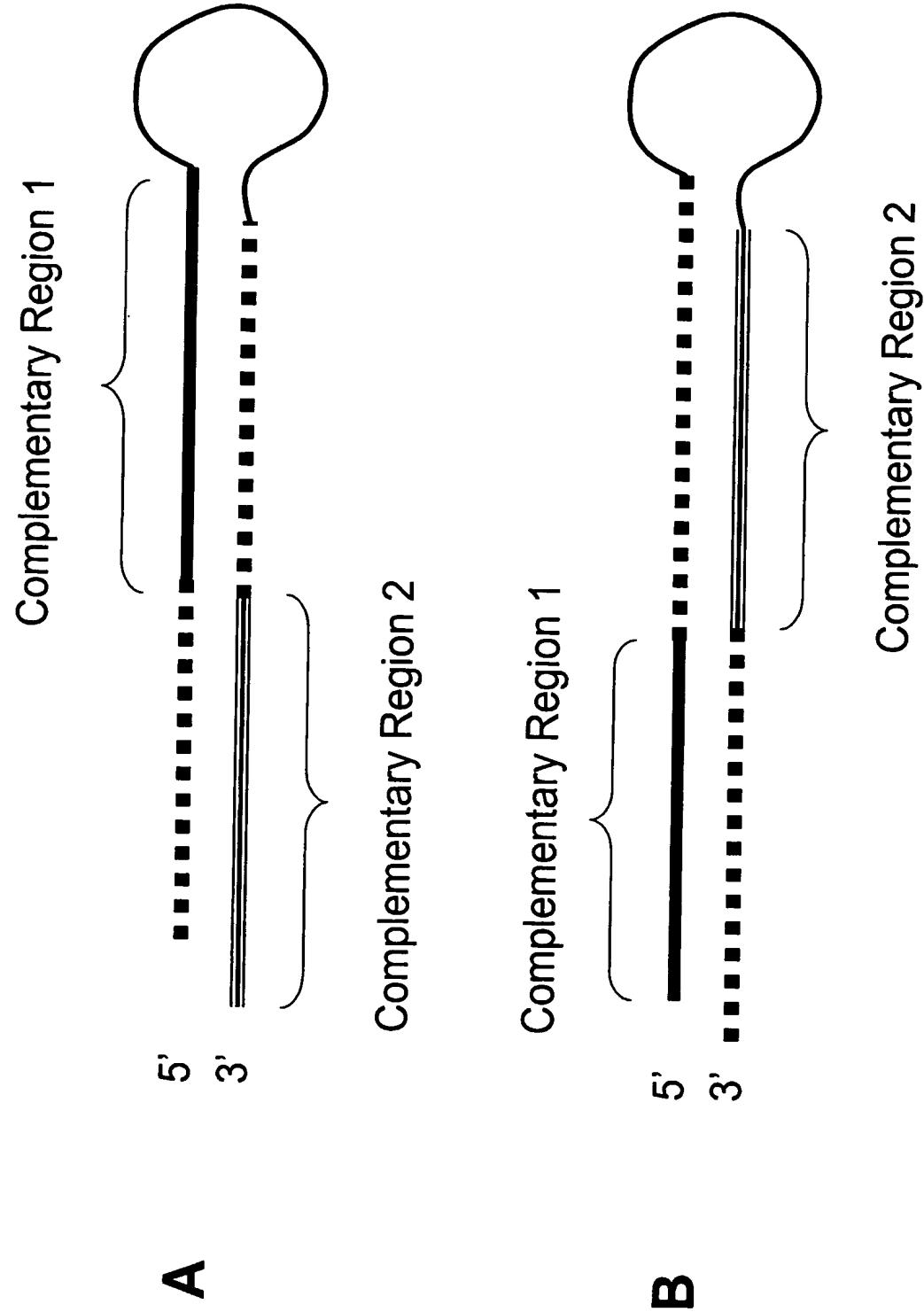


Figure 18: Examples of double stranded multifunctional siRNA constructs with distinct complementary regions and a self complementary/palindrome region

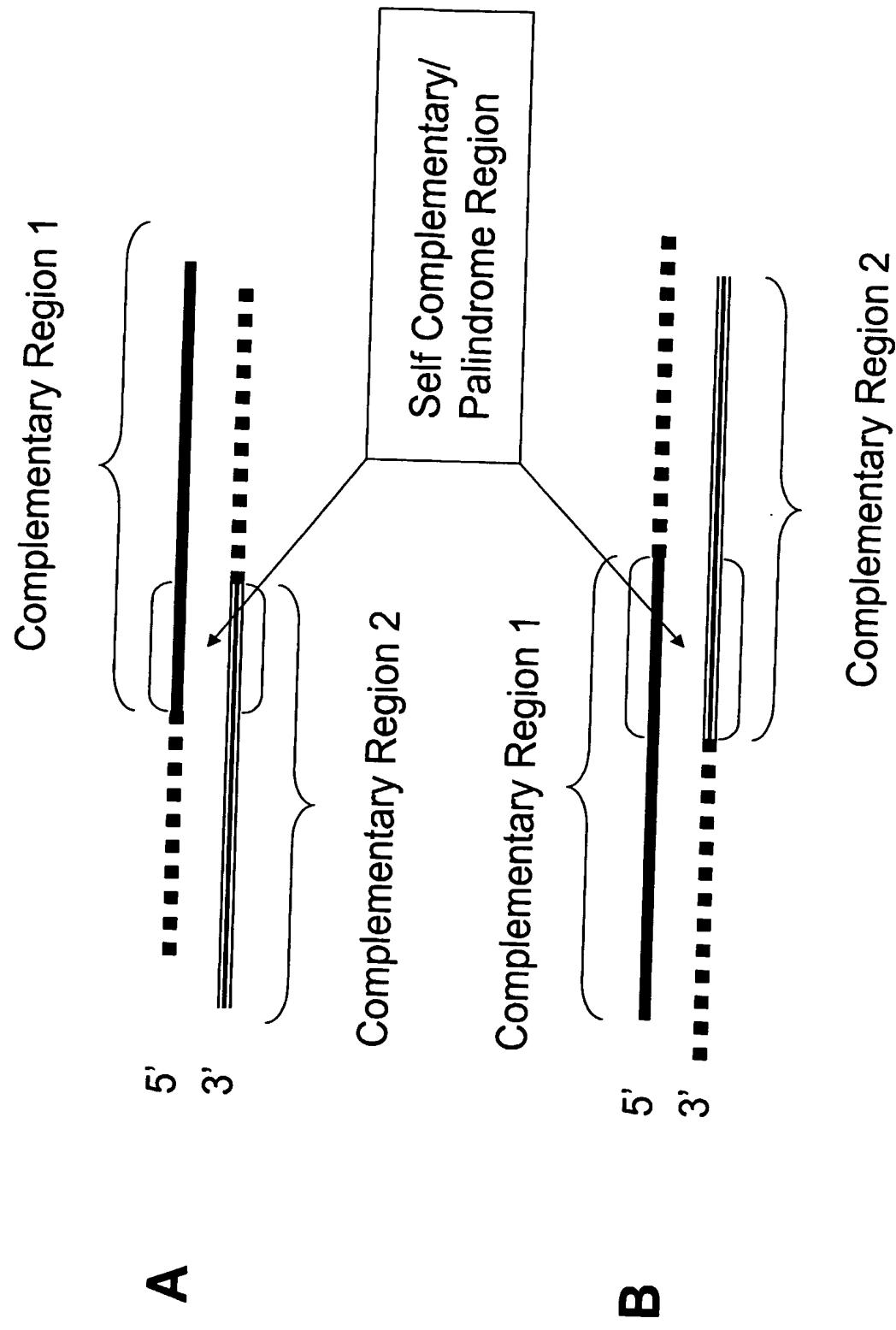


Figure 19: Examples of hairpin multifunctional siRNA constructs with distinct complementary regions and a self complementary/palindrome region

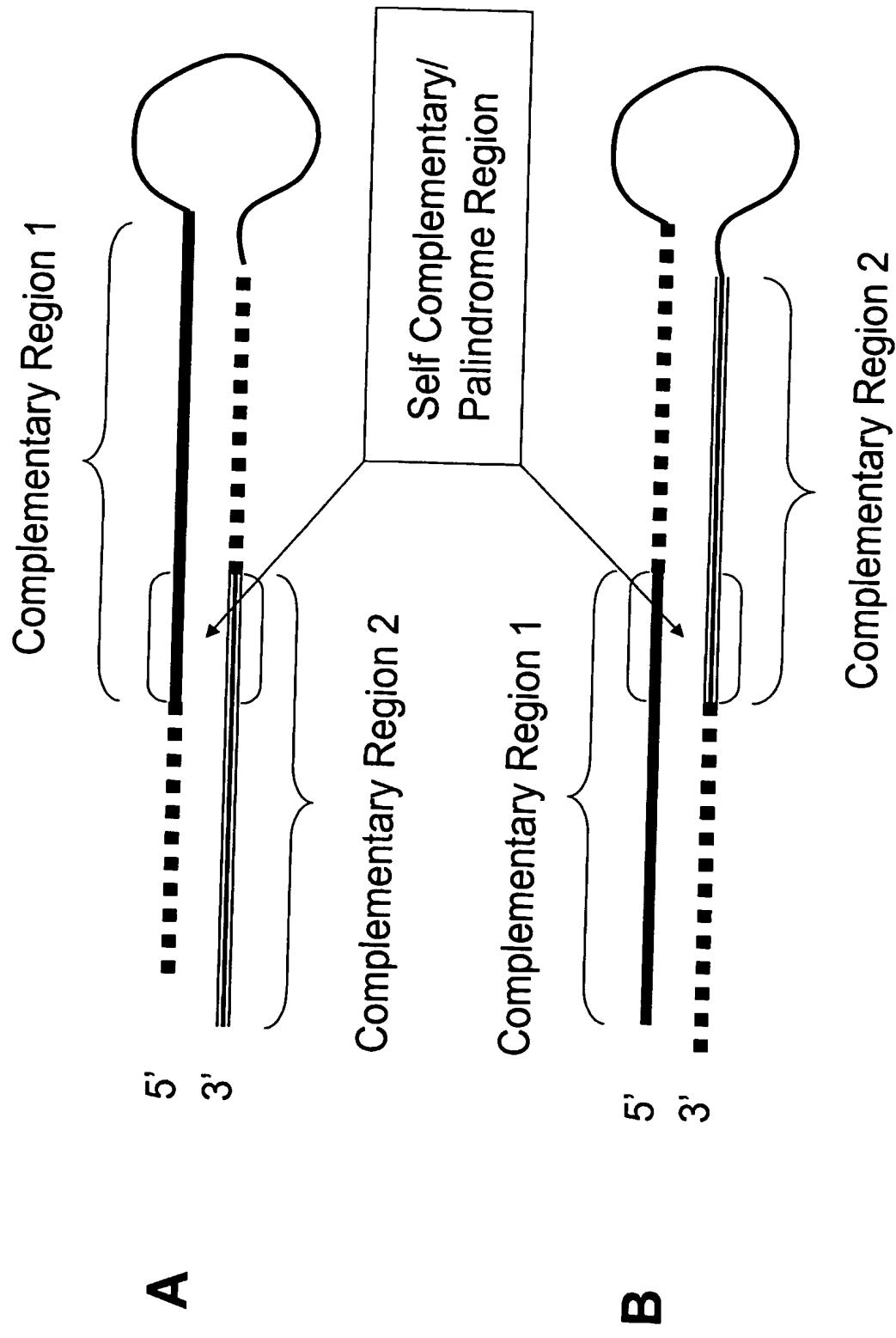


Figure 20: Example of multifunctional siRNA targeting two separate Target nucleic acid sequences

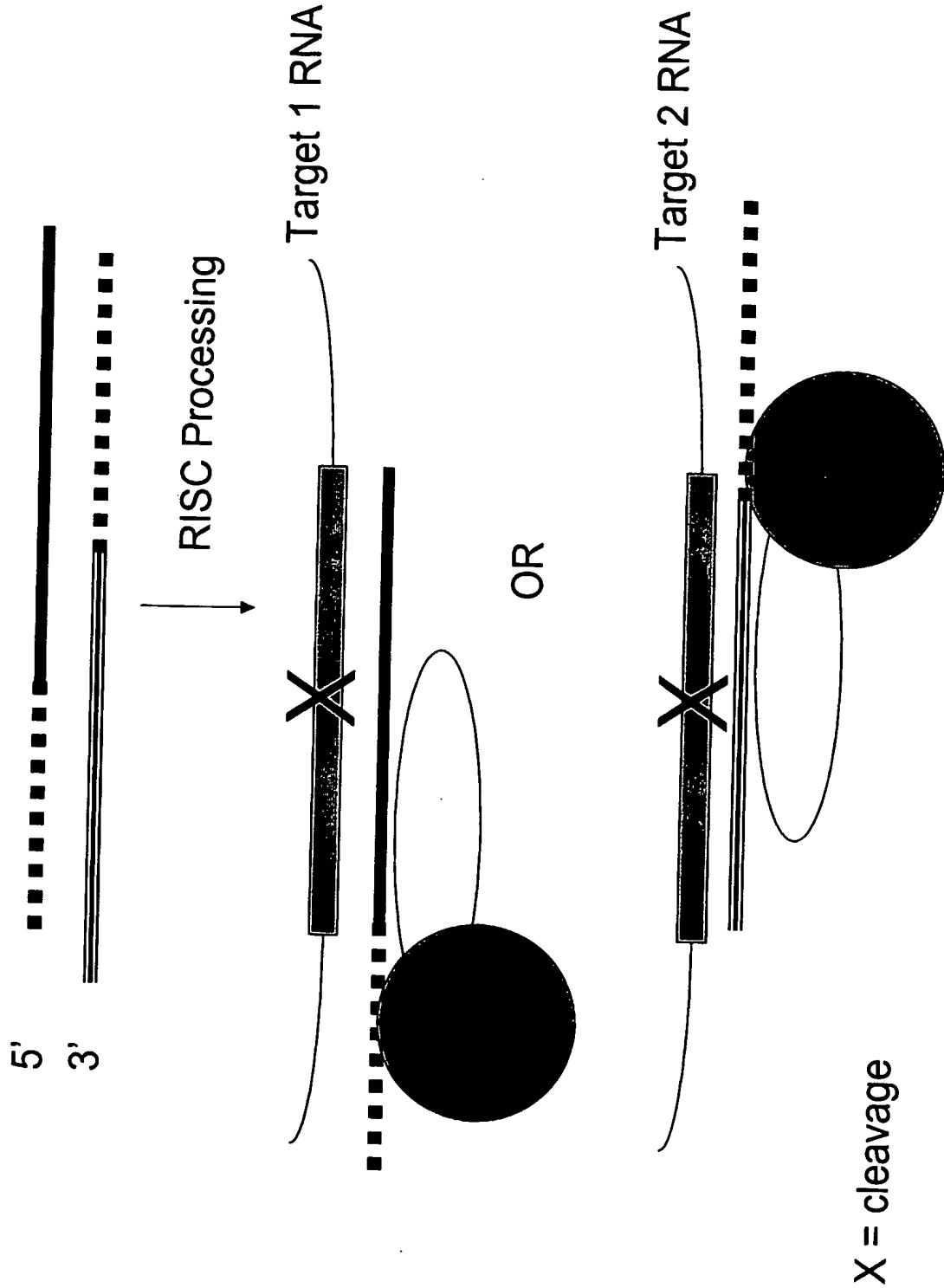


Figure 21: Example of multifunctional siNA targeting two regions within the same target nucleic acid sequence

